neuroleptic exposure, although a recent survey projected a risk of 68% after 25 years of exposure. Tardive dystonia carries a risk of only 1% to 2% but causes movements that are profoundly disabling and disfiguring. Some patients with tardive dystonia may benefit from therapy with the atypical neuroleptic clozapine, and many dystonic signs can be alleviated by periodic injections of botulinum toxin.

Although the incidence of the neuroleptic malignant syndrome has been a subject of debate, recent prospective studies suggest it is less than 0.1%. This life-threatening condition is characterized by hyperthermia and other autonomic instabilities, an altered mental state (from confusion through coma), rigidity and other extrapyramidal signs, and laboratory abnormalities, often including elevated creatine kinase levels and leukocyte counts. The neuroleptic malignant syndrome tends to occur early in the treatment course and with higher and more rapidly rising doses. The need for supporting vital signs in this condition is apparent, but the effectiveness of purported antidotes—namely dantrolene sodium, bromocriptine mesylate, and amantadine hydrochloride—has been contested.

Probably all neuroleptics lower the seizure threshold. This is not usually a problem, except when patients overdose, have underlying seizure disorders, withdraw from sedative-hypnotic agents, or take other proconvulsant medications. The use of clozapine, however, is associated with a relatively high incidence of seizures, particularly at higher doses. The incidence of seizures is 1% to 2% for doses of 300 mg per day, 3% to 4% for 300 to 600 mg per day, and 5% for 600 to 900 mg per day.

Although other antipsychotic drugs have rarely caused agranulocytosis, clozapine has been associated with about a 1% risk. Ashkenazi Jews may be at an elevated risk, and recent evidence suggests that HLA tissue typing may correlate with risk. If clozapine is stopped immediately and patients protected from intercurrent infection, full recovery can occur. The mechanism of agranulocytosis appears to be allergic rather than toxic, and patients must never be reexposed.

The administration of lower potency neuroleptics—most notably thioridazine hydrochloride and clozapine—is associated with electrocardiographic changes and can have clinical consequences. This is more likely to be a problem in overdoses, in patients with preexisting heart disease, or when neuroleptics are administered with drugs with comparable cardiac actions—such as quinidine-like effects, calcium channel blocking properties, or antiadrenergic activity.

Neuroleptics have been available for use for about four decades. They have been a godsend for many patients with chronic mental illnesses, and they have also alleviated nausea and gastroparesis in many others. Physicians prescribing these agents, however, need to be aware of their many, varied, and occasionally hazardous side effects. Clozapine has ushered in a new era of neuroleptic pharmacotherapy with powerful therapeutic benefits counterbalanced by serious toxicity. Over the next few years, we should see a new series of benzamides and other atypical neuroleptics that should broaden the ranges of both benefits and side effects.

ALAN J. GELENBERG, MD
Tucson, Arizona

REFERENCES

Glazer WM, Morgenstern H, Doucette JT: Predicting the long-term risk of tardive dyskinesia in outpatients maintained on neuroleptic medications. J Clin Psychiatry 1993; 54:133-139

Lieberman J, Saltz BL, Johns C, Pollack S, Borenstein M, Kane J: The effects of clozapine on tardive dyskinesia. Br J Psychiatry 1991; 158:503-510

Rosebush PI, Stewart T, Mazurek MF: The treatment of neuroleptic malignant syndrome—Are dantrolene and bromocriptine useful adjuncts to supportive care? Br J Psychiatry 1991; 159:709-712

Mitigating Posttraumatic Stress Disorder

FIRST ACKNOWLEDGED as a distinct diagnostic disorder with the 1980 publication of the *Diagnostic and Statistical Manual of Mental Disorders,* third edition, posttraumatic stress disorders are recognized today as valid and treatable psychiatric problems. Triggered by a traumatic event that is outside the range of usual and common human experience, symptoms manifest themselves as three clusters: the mental reexperiencing of the traumatic trigger event, the avoidance of sensory stimuli that have become associated with the trauma, and persistent hyperarousal of the autonomic nervous system.

Earlier research focused on identifying the characteristics of the trauma that stimulate posttraumatic stress disorder reactions and identifying specific risk factors. Survivors of natural disasters are more likely to have symptoms of reexperiencing the trauma, whereas those who have witnessed violence perpetrated by people are more likely to demonstrate avoidance and denial. Recently the contribution of genetic factors in individual vulnerability to posttraumatic stress disorder was shown in a study of 4,042 pairs of Vietnam-era monozygotic and dizygotic male twins. Posttraumatic stress disorder-spectrum symptoms in monozygotic pairs with exposure to combat were more highly concordant.

Symptom intensity in this complex group of disorders is the result of the interaction of many genetic and environmental factors. Their relative contributions await further study, but it holds that improving what is improvable, namely, a person's environment, can have a profound ameliorating effect on the development and the course of these disorders.

There is immense practical value to a health care system facing the prospect of massive casualties to train triage physicians to recognize psychological traumas. The patients suffering acute traumatic stress disorders can be diverted to a nonhospital treatment site that does not reinforce the sickness role. This also frees up hospitals and their medical personnel to concentrate on treating patients needing urgent surgical therapy. During the Persian Gulf War, about 43% of patients admitted to a hospital following Scud missile attacks on Israeli cities had purely psychological trauma. Secondary triage to separate patients with psychological trauma from those with physical injuries lessens the burden on a stressed emergency care system.

Trauma survivors are faced with shattering realities: the loss of a sense of safety and stability, an awareness

that they can easily be rendered totally helpless by circumstance, and a forced confrontation with their own mortality. "Secondary wounding" with extension of the trauma can occur when medical and other caregivers manifest attitudes that suggest disbelief or blaming the patients for causing their own trauma. Implications that trauma survivors should have been more cautious, more intelligent, more resistant, or more morally outraged tend to be directed particularly to the victims of human-caused disasters. This unnecessary worsening of the original trauma, when based on a health worker's ignorance, burnout, or personal belief system, can be avoided. Secondary wounding can also occur at the hands of fellow trauma survivors, who happen, at that point in time, to be coping with their own losses by the use of denial of the adverse consequences.

A natural result of primary and secondary trauma is internalization of the victim status. Though no longer in a traumatic situation, such patients adopt the disaster and its aftermath as the central, dominating event in their lives. They then use it to determine their general worldview and the way they think and act. Secondary prevention efforts must address these attitudes that underlie the "permanent victim" status: intolerance of one's mistakes and fear of seeming defective, weak, or cowardly. Research has shown that primary prevention in the form of rapid, brief psychiatric intervention and the use of support groups can minimize the development of persistent posttraumatic stress disorder symptoms. The short-term use of benzodiazepine or antihistamine agents with anxiolytic or hypnotic effects can be helpful in selected patients not prone to chemical dependency.

KATHLEEN BELL UNGER, MD
San Francisco, California

REFERENCES

Bleich A, Dycian A, Koslowsky M, Solomon Z, Wiener M: Psychiatric implications of missile attacks on a civilian population—Israeli lessons from the Persian Gulf War. JAMA 1992; 260:613-615

Psychosocial Consequences of Disasters—Prevention and Management. Geneva, Switzerland, World Health Organization Division of Mental Health, WHO publication No. WHO/MNH/PSF/91.3, 1992

Sexual Victimization and Physical Symptoms in Women

THERE IS A GROWING AWARENESS that childhood sexual abuse causes not only psychological sequelae but also continuing medical morbidity. Sexual victimization can be associated with several long-term physical effects.

Several recent, well-designed studies have associated sexual victimization with a variety of medical conditions, particularly chronic pelvic pain and the irritable bowel syndrome. Surveys of participants of health maintenance organizations have also shown increased rates of smoking, obesity, excessive alcohol and drug use, pregnancy before age 18, abortions, multiple sex partners, high-risk sexual contacts, a greater number of unintended pregnancies, earlier first intercourse, and a decreased frequency of Pap smears for survivors. They have also been shown to be higher users of medical care resources, averaging two to three times the usual rates of clinic attendance.

The health care use of survivors may also be influenced by social and psychological factors. A higher use may arise from the inability of a woman's family of origin to protect her from the abusive relationship or to provide early medical intervention and ensuing psychological care. Subsequent contacts with health care professionals may afford opportunities for the survivors to obtain this emotional support from their medical caregivers, thus reinforcing somatization and increased health care use.

The Council on Scientific Affairs of the American Medical Association has recently issued a special report declaring the need for an increased awareness on the part of physicians of all forms of violence against women. The report suggested guidelines for physician training in assessing past victimization as part of the routine care of women. Given the prevalence of sexual victimization, it is likely that physicians come into daily contact with a substantial number of sexual victimization survivors. Greater awareness of the long-term biopsychosocial effects of sexual victimization may be a critical aspect of improving care for these patients.

EDWARD A. WALKER, MD
Seattle, Washington

REFERENCES

Drossman DA: Sexual and physical abuse and GI disorders in women: What is the link? Emerg Med Clin North Am 1992; 24:171-175

Fry R: Adult physical illness and childhood sexual abuse. J Psychosom Res 1993; 37:89-103

Walker EA, Katon WJ, Hansom J, et al: Medical and psychiatric symptoms in women with childhood sexual abuse. Psychosom Med 1992; 54:658-664

Role of Newer Antidepressants

NEWER ANTIDEPRESSANTS are gradually replacing old tricyclic antidepressants because of comparable efficacy with fewer side effects and a much lower risk of death from overdose. Newer-generation antidepressants include trazodone hydrochloride, bupropion hydrochloride, and the selective serotonin reuptake inhibitors fluoxetine hydrochloride, sertraline hydrochloride, and paroxetine.

Trazodone and bupropion, unlike tricyclic antidepressants, are ineffective for panic. Anticholinergic effects—dry mouth, blurred vision, constipation, and urinary retention—and cardiovascular effects are less with the newer drugs than with tricyclic antidepressants. Weight loss can occur with bupropion and fluoxetine. Overdose lethality is rare with these newer drugs.

Newer antidepressants, like tricyclic antidepressants, show efficacy at two to six weeks, and about 50% to 70% of depressed patients obtain benefit. Patients who partially respond or do not respond may benefit from lithium or triiodothyronine augmentation or by changing to a different class of drug, such as from trazodone to serotonin reuptake inhibitors and serotonin reuptake inhibitors to bupropion.

Trazodone is highly sedating, and dose titration to the maximum tolerated dose is required in the 100-mg to 600-mg at bedtime range based on daytime sedation. Trazodone, 50 mg to 100 mg, is widely used as a hypnotic in lieu of potentially addicting medications. It may wors-